

THE RIGHT LUNG OF A HUMAN FOETUS OF 152 MILLIMETERS, C. R., LENGTH

DWIGHT M. PALMER,
Department of Anatomy, Ohio State University

I. INTRODUCTION

According to the classical accounts, the lower respiratory passages, beginning at the larynx and extending caudally to and including the pulmonary aveoli, develop from a branching diverticulum that has its origin from the entoderm of the floor of the foregut.

The earliest indication of the formation of these respiratory passages in the human embryo is a deep groove that appears on the inner aspect of the ventral surface of the primitive pharynx and oesophagus. Externally the same area presents a longitudinal ridge. Such a stage has been described in an embryo 2.5 millimeters in length by Heiss (1). As development continues the posterior end of the groove becomes a deep globular pocket. This pocket and the posterior end of the groove become a locus of rapid growth and so appear to be cut off from the more dorsally placed foregut. This apparent detachment proceeds in a cephalic direction. The globular pocket evaginates on either side and becomes bilobed. These lateral enlargements are known as the right and left stem buds.

The stem bud is the anlage of the stem bronchus. The latter structure represents the main axis of growth in the developing bronchial system and it becomes the large bronchus, which, arising from the trachea on each side, passes into the hilum and through the pulmonary substance almost to the periphery of the lung. In its course the stem bronchus gives off a series of branches known as the lateral bronchi. These branches arise as evaginations or buds from the region of the growing blind tip of the stem bronchus. The larger and more numerous of these so-called lateral bronchi are given off ventral to the main stem of the pulmonary artery as the latter structure accompanies the stem bronchus. Aeby (2) designated this group of branches as ventral bronchi while other authors have called them lateral bronchi. Smaller and less numerous branches arise dorsally from the stem bronchus and are called

dorsal bronchi. Occasional small branches arising from the stem bronchus in intermediate positions either medial or ventral have been described.

According to Narath (3) three of these branch bronchi are present in a human embryo 7.0 millimeters long. These are the right first lateral bronchus (ventral according to his terminology), the left first lateral (ventral) bronchus and the right apical bronchus. The latter bronchus was regarded as a special type and was termed the eparterial bronchus by Aeby because it arises above the pulmonary artery in contrast to all the other bronchi which are hyparterial in origin. However, Narath held that it was the first dorsal bronchus on the right side. Huntington (4) states that except for purposes of topography we should abandon the distinction between eparterial and hyparterial bronchi. In this description of the right lung the right apical bronchus will be referred to as D1.

Other bronchi arise successively from the growing stem bronchus until there are four or five lateral bronchi (L1, L2, L3, L4, etc.) and two to four dorsal bronchi, (D1, D2, etc.). All of these are generally classed as secondary bronchi. A new generation, tertiary bronchi or bronchi of the third generation, bud outward from the secondary bronchi. From the tertiary bronchi another generation, the quaternary bronchi develop and in turn a fifth generation of tubules grow out from the quaternary group. Arey (5) quotes Broman as stating that there are in all eighteen generations of pulmonary branchings at birth.

In addition to the evaginations that appear near the tips of the growing buds, new bronchi of the later generations may arise from the blind tips by a splitting of the tip into two or three tubules of the next generation. Since the tubules of the respiratory passages arise by combinations of these methods of formation of new divisions a branching system evolves which becomes more and more like a tree.

While the general plan of development of this tracheo-bronchial tree is fairly constant, variations usually minor in character may occur. However, Davis (6) states that to his knowledge no other organ has so varied an arrangement of one of its fundamental structures (bronchi).

The budding bronchi grow out into a mass of mesenchyme. This mesenchymal tissue does not contribute to the formation of the lower respiratory passages.

In the last few years the classic concept of the embryology of the lung, so briefly reviewed here, has been questioned by a number of authors—Rose (7), Policard (8), Chiodi (9), Dogliotti (10), Faure-Fremiet (11), Stewart (12). The majority of the conflicting opinions center on the development of the terminal portions of the tracheo-bronchial tree and particularly on the origin and nature of the lining of the atria, air-sacs and alveoli of the adult lung.

Grosser (13) states that a number of important questions concerning the embryology of the human lung have not been settled, partly because the necessary material has not been available. It would seem that a detailed report of the anatomy of the lung of a human foetus just prior to the period of viability might be valuable as a basis for further studies.

In anticipation of a study of the tracheo-bronchial tree in the latter months of the human foetal period the author has examined the tissues of a human foetus which was aborted at about the nineteenth week of prenatal life. These tissues were found to be in an excellent state of fixation.

II. MATERIAL AND METHODS

Material.—Case History: The mother knew that she had been pregnant at least three and one-half months. She was admitted to the hospital with a complaint of vaginal bleeding which had begun following a fall that had occurred three weeks before. However, there were no signs of active hemorrhage on admission. The urinalysis and blood Wassermann test were both negative. On examination the abdomen was found to be somewhat larger than that usually seen in a pregnancy of three and one-half months duration. The foetal heart rate—153 beats per minute was distinctly heard in the left lower quadrant of the abdomen. Seven hours after the admission of the mother to the hospital the foetus was spontaneously expelled. On examination of the foetus the heart could be heard, per stethoscope, but there were no signs of any respiratory movements. A short time later there were no signs of life in the foetus and it was pronounced dead.

The foetus was of the male sex. The skin was moderately firm and no abnormalities were noted. The crown rump measurement or sitting height of the foetus was 152 millimeters. According to the formulae and charts given in standard textbooks of embryology, this measurement would place the foetus

in the nineteenth week of prenatal life. The foetus was placed in 10% formalin for forty-eight hours. At this time the anterior thoracic wall was partly removed and the pleural sacs opened. Then the foetus was placed in a fresh formalin solution. Later the lungs were observed and sketched in situ. In order to avoid many technical difficulties it was decided to make a study of only one lung. The right lung was chosen as the material to be investigated because the more complex problems of morphogenesis have centered on that lung.

Methods.—The trachea, primary bronchi, right lung and vessels, thoracic aorta, thoracic duct and thoracic portion of the oesophagus were removed en masse. The tissues were washed, dehydrated and embedded in paraffin. Serial sections of the entire mass, 20 micra in thickness, were prepared and stained with hematoxylin and eosin.

Several wax reconstructions were made by projecting the stained sections upon 2.0 millimeter beeswax plates by use of an Edinger Drawing and Projection Apparatus.

A model of the entire lung magnified to five diameters was constructed to show the distribution of the bronchi. (Plate I). A model of the stem bronchus and the origin of its branches, magnified one hundred diameters was prepared. After the stem bronchus of the lung had been modeled to its termination, one of its end branches was followed along the principal axis to its subpleural termination on the diaphragmatic surface of the lung. As the termination of this branch was approached a three-way branching was encountered. From this point outward all the divisions and subdivisions of this branching were modeled. This included an ovoid mass of pulmonary tissue that was separated from the remaining pulmonary tissue as a lobule by thin strands of connective tissue containing branches of the pulmonary vein. Other models of portions of the tracheo-bronchial tree were constructed in attempting to enumerate the number of generations of bronchi that are present in different areas of the lung.

The volume proportion of the epithelial tubules to the stroma was determined by projecting representative fields upon sheets of heavy white paper. The tubules were outlined on the paper and the sheet was weighed. Then the tubule outlines were cut out and the remaining paper weighed.

III. MORPHOLOGY

A. THE LUNG AS A WHOLE

The lung was of a uniform yellowish-white color. The chief differences noted in the appearance of this lung and that of an adult right lung were that the foetal lung was shorter from apex to base and that the cardiac impression was relatively large. The superior and middle lobes were continuous for a distance of five millimeters lateral to the anterior border, the transverse interlobar fissure being incomplete in this area and absent on the mediastinal aspect. The fine lobulations of the pulmonary tissue were plainly visible beneath the glistening transparent visceral pleura.

After fixation the lung measured 19 millimeters in vertical height (from apex to center of base). The base measured 26 millimeters in its longest antero-posterior diameter and 16 millimeters in its longest transverse diameter.

B. THE TRACHEO-BRONCHIAL TREE

1. *Trachea and Stem Bronchi.*

(a) The trachea has a position similar to that which it occupies in the adult. It is slightly compressed from anterior to posterior and the posterior surface is flattened. The lumen has a diameter of about 1.7 millimeters. The trachea terminates inferiorly by dividing into right and left stem bronchi (primary bronchi).

(b) The left stem bronchus makes a less obtuse angle with the trachea than does the right stem bronchus. The lumen of the left stem bronchus has a diameter of 1.0 millimeter.

(c) The right stem bronchus passes inferiorly and laterally after its origin at the bifurcation of the trachea. Its borders are rounded with the exception of the posterior which is flattened. Just below its origin the greatest diameter of the lumen is 1.2 millimeters. This stem bronchus gives rise to three dorsal, three lateral, one ventral and two terminal branches. The bronchial pattern formed by the right stem bronchus is as follows: D1, L1, D2, V1, L2, D3, L3, D4 and L4, respectively, from the oral end outward.

As the stem bronchus approaches the medial surface of the superior lobe a large branch is given off laterally. This is the first dorsal bronchus, D1. It arises 4.0 millimeters from the bifurcation of the trachea. The pulmonary artery lies infero-medial to the origin of D1. At a lower level the artery gives off a branch which passes anterior to the stem bronchus, then laterally and superiorly to be distributed with D1. At this second level the main stem of the pulmonary artery lies antero-medial to the stem bronchus.

The stem bronchus now passes inferiorly and laterally with the pulmonary artery being found successively antero-medial, anterior and antero-lateral. Both structures now lie well within the hilum of the lung. A large branch, L1, arises from the antero-medial aspect of the stem bronchus about 6.9 millimeters from the angle of bifurcation of the trachea. At approximately the same level a small bronchus, D2,

arises from the posterior aspect of the stem bronchus and passes postero-laterally into the hilum portion of the inferior lobe.

The stem bronchus now becomes definitely incorporated in the inferior lobe. The next branch arising from the stem bronchus is a large ventral one, V1, which has its origin 8.7 millimeters from the bifurcation of the trachea. The stem bronchus then passes postero-laterally as well as inferiorly. The next bronchus arising from the stem bronchus is a lateral branch, L2. According to Narath the dorsal bronchi are usually fewer in number than the ventral bronchi. L2 arises 10.4 millimeters from the tracheal bifurcation.

A small dorsal bronchus, D3, arises posteriorly from the stem bronchus, 11.9 millimeters from the tracheal bifurcation. At the same level a ventral branch, L3, is given off antero-laterally. After passing posteriorly and inferiorly the stem bronchus terminates by dividing into two bronchi, a smaller postero-medial, D4; and a larger antero-lateral bronchus, L4. This point of termination is 13.0 millimeters from the trachea.

When the right stem bronchus is viewed from above, as from the position of the trachea, a definite spiral curvature is noted in its course. This curvature is clockwise in direction when viewed from the above mentioned position. A similar curvature is present in the course of some of the branches of the stem bronchus, being especially well marked in the fourth lateral bronchus. In the latter case the branches of L4 arise in alternating planes which are at right angles to each other; that is one branch is given off in a transverse plane and the next in an antero-posterior plane.

2. *Bronchi Arising Directly from the Stem Bronchus.*

(a) D1. (Apical Bronchus, Eparterial Bronchus.)—This bronchus arises from the lateral side of the stem bronchus and passes laterally and slightly anteriorly into the hilum portion of the superior lobe. About 0.6 millimeters from its origin, D1 gives off a large posterior branch, D1p, which gives origin to all the bronchi which supply an area bounded by the posterior one-fourth of the costal surface and all of the oblique fissural surface of the superior lobe. (Plate I.) The terminal tubules from this posterior branch reach almost to the apex of the superior lobe. D1 then passes inferiorly and antero-laterally giving off a series of branches. These branches supply the remainder of the superior lobe, namely, an area bounded by the mediastinal, transverse fissural and anterior three-fourths of the costal surface of the superior lobe.

(b) L1. (Bronchus to Middle Lobe—First Lateral Bronchus.)—L1 gives origin to all the tubules found in the middle lobe of the right lung. This bronchus arises from the antero-medial aspect of the stem bronchus as the latter lies in the hilum of the lung. The main stem of the pulmonary artery is lateral to L1 at the point of origin of the latter from the stem bronchus. L1 passes inferiorly, anteriorly and somewhat laterally entering the hilum portion of the middle lobe. At this point L1 gives off a large posterior branch, L1p, then passes downwards and forwards and gives origin to all the bronchi found in the area bounded

by the mediastinal surface, antero-medial four-fifths of the diaphragmatic surface, and anterior two-fifths of the costal surface of the middle lobe. The posterior branch passes downwards, laterally and slightly forwards and supplies all the bronchi found in the remainder of the middle lobe, namely, the area bounded by the postero-lateral one-fifth of the diaphragmatic surface, the lateral three-fifths of the costal surface and by the surface facing into the oblique interlobar fissure.

(c) D2. (Second Dorsal Bronchus.)—This bronchus arises in the hilum of the lung from the posterior aspect of the stem bronchus. The lumen of D2 measures 0.6 millimeter in diameter. The second dorsal bronchus passes postero-laterally into the hilum portion of the inferior lobe about 5.3 millimeters below the most cranial or apical portion of that lobe. D2 arises posterior to the main stem of the pulmonary artery and the branch of that artery which is distributed with D2 lies along the lateral side of the latter structure. D2 almost immediately gives off a posterior branch which gives origin to the bronchi found in the area bounded by posterior half of the costal surface of the inferior lobe from the apex extending downward for about 7.0 millimeters. After giving origin to this posterior branch, D2 continues downwards and laterally giving origin to the bronchi of the inferior lobe in the area antero-medial to that supplied by the posterior branch. The lower limit of the bronchial distribution of D2 may be marked by a line which is almost transversely placed but which is slightly higher along the vertebral margin of the lung and curves across the costal surface to within a millimeter of the oblique interlobar fissure, then turning somewhat upwards to meet the fissure.

A marked similarity is noted in the location of site of origin from the stem bronchus, the branchings and the areas supplied by bronchi D1 and D2. The mass of lung supplied by D2 is in fact a miniature of the superior lobe, which is supplied solely by D1. Such a similarity, although less marked, will be pointed out between bronchi L1 and L2.

(d) V1. (First Ventral Bronchus—Infra-cardial Bronchus.)—This bronchus arises from the antero-medial aspect of the stem bronchus. At the site of origin V1 is medial to the main stem of the pulmonary artery. The lumen of V1 has a diameter of 0.5 millimeter. V1 passes directly downward into the hilum portion of the inferior lobe and gives off a lateral branch, then continues downward into the antero-medial portion of the inferior lobe. The first ventral bronchus supplies all the bronchi found in an area bounded by the mediastinal surface of the inferior lobe below the hilum and by the antero-medial two-fifths of the diaphragmatic surface of the inferior lobe.

(e) L2. (Second Lateral Bronchus.)—This bronchus arises from the lateral portion of the anterior aspect of the stem bronchus. At its site of origin L2 lies medial to the main stem of the pulmonary artery. The lumen measures slightly over 0.4 millimeters in diameter. L2 passes downwards, forwards and laterally and gives off a large lateral branch. Then it continues downwards and forwards. The second lateral bronchus supplies a wedge-shaped segment of the inferior lobe below the level of the hilum. The surfaces of this segment are a vertical strip of the costal surface along the oblique inter-lobar fissure, the

lateral half of the surface facing into the fissure and the antero-lateral one-fifth of the diaphragmatic surface.

In lower animals the lung is clearly made up of a series of supra-imposed tiers, each tier being supplied by a dorsal bronchus and its fellow lateral bronchus with the accessory bronchi that may be present at that level. In the human lung this system of tiers while not so distinct may still be traced by referring to the various views of the model prepared to show the distribution of bronchi (Plate 1). Each successive tier lies medially, inferiorly and posteriorly to the preceding tier. The first tier has far outgrown the others, forming the superior and middle lobes. The portion of the lung constituting the second tier supplied by D2, V1 and L2 is somewhat of a miniature of the superior and middle lobes supplied by D1 and L1, respectively.

(f) D3. (Third Dorsal Bronchus.)—This bronchus arises from the posterior aspect of the stem bronchus as the latter lies deep in the interior of the inferior lobe. D3 passes directly backwards into the inferior lobe posterior to the main stem of the pulmonary artery. The lumen of D3 has a diameter of 0.2 millimeter. The third dorsal bronchus supplies a wedge-shaped segment of the inferior lobe. This segment is flattened from above downwards and has its base on the middle portion of the costal surface of the inferior lobe.

(g) L3. (Third Lateral Bronchus.)—This bronchus arises from the antero-lateral aspect of the stem bronchus medial to the main stem of the pulmonary artery. The lumen of L3 measures 0.4 millimeter in diameter. L3 passes downwards and laterally, gives off a postero-lateral branch and then continues downward. The third lateral bronchus is distributed to a wedge-shaped segment of the lower half of the inferior lobe. This segment borders on the postero-lateral portion of the costal surface and on the postero-lateral one-sixth of the diaphragmatic surface of the inferior lobe.

(h) D4. (Dorso-Medial Terminal Branch of Stem Bronchus.)—The lumen of this bronchus measures 0.4 millimeter in diameter. The bronchus passes postero-laterally and inferiorly and is distributed to a tetrahedral segment of the lower half of the inferior lobe. The base of this segment is on the postero-medial portion of the costal surface.

(i) L4. (Antero-Lateral Terminal Branch of Stem Bronchus.)—The lumen measures 0.6 millimeter in diameter. L4 passes inferiorly and is distributed to a wedge-shaped segment of the lower half of the inferior lobe. This segment borders on the most convex portion of the costal surface and on the posterior one-fifth (approximately) of the diaphragmatic surface.

3. *Branches Arising from the Direct Branches of the Stem Bronchus.*

It seems questionable whether all the direct branches of the stem bronchus should be classed as secondary bronchi. The report of Narath on the morphology of the bronchial system in a human embryo of 7.0 millimeters in length seems to justify the application of the term secondary bronchus or bronchus of the second generation to D1 and L1 since they apparently arise proximal to the growing tip of

the stem bronchus. Whether the remaining branches of the stem bronchus should be classed as secondary bronchi remains a problem until a larger series of early human embryos have been studied. This same lack of a more complete series prohibits the classification of the branches of D1 and L1 as secondary stem bronchi with tertiary branches although such a pattern seems to be common to each of them. However, in each of these bronchi the first branch is a posterior one and is almost as large as the parent secondary bronchus which continues on from the site of origin of the branch. From the bronchi arising from the stem bronchus and from the branches of these bronchi many generations of tubules arise. As yet there seems to be no exact way of determining what generations of these will develop into the bronchi and bronchioles of the adult lung. Following the example of Kolliker (14) we may denote all the branches as tubules. The determination of the exact number of generations of tubules present in the simple tracheo-bronchial tree of a young embryo is a difficult problem, and the difficulties are greatly multiplied in the study of the tree in a foetus in the nineteenth week of prenatal life. It is fairly well agreed that new tubules may arise by any one or by combinations of three methods, namely, lateral budding (monopodial), dichotomous branching and trichotomous branching. No definite regularity in the appearance of these methods of tubule formation has been described. Furthermore, in examining an embryological specimen it should always be remembered that the growth processes may have obscured the forms of an earlier stage. A dichotomous branching may later appear to be a larger bronchus giving off a smaller side branch due to more rapid growth in one of the pairs of bronchi previously formed by the dichotomous division.

It is apparent that a definite rule is necessary before determinations of value can be obtained. Accordingly the following rules have been observed in making the determinations of the number of generations of tubules present in the different lung areas listed. First, some type of reconstruction or models should be prepared from a complete set of serial sections. A model is necessary so that no branches will be overlooked, and is especially desirable in studying the finer ramifications where new tubules arise from many aspects of the parent stems.

Second, when tracing along a tubule and its first branch is encountered, that branch should be given a number denoting the succeeding generation. Then this branch is traced along its course and the tubule previously being traced is disregarded. This branch is followed until its first branch is found and then this latter branch is given a number denoting another generation and it is followed, etc. If a division with branches of equal size is found, the one that is distributed to the more orally located area is assumed to be the branch.

This method seems reasonable and necessary because it is an assumption to treat a small bronchus as a branch of a large bronchus in every case, whereas the two may have at an earlier period been fellow members of a dichotomous branching, after which one (the assumed main bronchus), grew more rapidly. Using these rules the following results were obtained:

Superior Lobe.—Considering D1 as a secondary bronchus (generation 2) there are sixteen generations of tubules present.

Middle Lobe.—Considering L1 as of generation 2 there are seventeen generations of tubules present. In the particular region examined the seventeenth generation was just in the process of formation, being represented as paired evaginations of the blind end of the preceding tubule, (generation 16).

Inferior Lobe.—The number of generations of tubules arising from the remaining dorsal bronchi was determined by the same method. If these bronchi (D2, D3 and D4) are considered as bronchi of the second generation the results are: D2, 15 generations; D3, 14 generations; D4, 13 generations. It is interesting to note the progressive decrease in the number of generations from the successive dorsal bronchi. It suggests a correlation with the tier structure of the lung that is so much more apparent in lower animals. However, D2, the dorsal representative of the second tier, may be considered a bronchus of the third generation and then the number of generations in this area will be 16, the same number as was found in the area of D1.

The first seven or eight generations of bronchi lie within definite connective tissue septa while the remaining generations lie within and largely make up the areas inclosed by less distinct septa.

C. LUMINA

In the first seven or eight generations, whose walls are rigid, the margins of the lumina are markedly serrated due to the longitudinal foldings of the inner coats of the bronchi. In the remaining generations the lumen is small but usually distinct. The lumen in these latter tubules is greatest at the site of origin of branches and at the blind ends of the tubules. These terminal expansions do not appear to be as large relatively as the terminal buds observed at earlier periods in the development of the tracheo-bronchial tree. Merkel (15) quotes Kolliker as stating that air-cells begin to be formed in the sixth month of foetal life and that in the beginning of the fifth month the end buds measure 0.09 to 0.13 millimeter in diameter.

In this foetus the following diameters were found for the lumina of two sets of generations of bronchi: (diameters in millimeters).

Generation	D1	L1	Generation	D1	L1
2.....	.70	.60	10.....	.08	.08
3.....	.41	.46	11.....	.07	.06
4.....	.29	.35	12.....	.05	.06
5.....	.26	.28	13.....	.05	.05
6.....	.18	.14	14.....	.03	.03
7.....	.11	.12	15.....	.03	.03
8.....	.09	.09	16.....	.04	.03
9.....	.09	.09	17.....03

These measurements are of only one successive line of tubules in the respective areas. The size of the tubules of one generation is variable among the larger tubules but the terminal generations are of a uniform size throughout the lung, the lumen averaging about 0.03 millimeter and the entire tubule 0.05 millimeter in diameter.

D. BLOOD VESSELS

1. *The Pulmonary Artery.*

The right branch of the pulmonary artery passes directly laterally from its origin and then turns downward in front of the stem bronchus at a point just inferior to the origin of bronchus D1. The lumen of the artery has a diameter of 1.4 millimeters. Corresponding to the bronchi the main arterial trunk or stem artery gives origin to a branch for each bronchus that arises from the stem bronchus. The arterial branches arise at a slightly higher level than the bronchi which they accompany but are given off in a plane exactly parallel to the plane in which the bronchus arises. The arterial branches pass outward on the lateral aspect of their corresponding bronchi.

2. *The Pulmonary Veins.*

The small venous channels lie between the pulmonary lobules. The upper pulmonary vein drains the superior and middle lobes, the vein from the superior lobe passing anterior to both the stem artery and the stem bronchus while the veins from the middle lobe converge to form a trunk that lies medial to the first lateral bronchus. The lower pulmonary vein, draining the inferior lobe, lies posterior to the stem artery and the stem bronchus.

3. *Bronchial Vessels.*

The bronchial arteries are very small and together with the bronchial veins are found lying on the posterior aspect of the stem bronchus.

E. LYMPH GLANDS

There are two tracheo-bronchial lymph glands present, the largest measuring 1.1 by 1.8 millimeters in cross-section. There were probably other members of this particular group of glands that were not removed from the thorax. There are four intertracheo-bronchial glands (glands of the bifurcation) and nine broncho-pulmonary glands present. No members of the pulmonary group of lymph glands were observed.

F. NERVES

The right vagus nerve lies longitudinally along the right postero-lateral aspect of the trachea. From this nerve a large branch passes along the posterior surface of the stem bronchus into the hilum of the lung. Here it breaks up into smaller branches which accompany the bronchi arising from the stem bronchus. Nerves could not be traced beyond the fifth generation of tubules. A specific nerve stain was not employed. One or two other small nerves are present in the outer wall of the stem bronchus, but their exact origin was not determined.

IV. HISTOLOGY

A. THE TRACHEO-BRONCHIAL TREE

1. *Epithelium.*

The epithelium of the oral end of the tracheo-bronchial tree is of a ciliated pseudo-stratified columnar type containing the same four types

of cells as the epithelium of the adult trachea; namely, basal, intermediate, ciliated and goblet cells. A typical cuticular border is present. The goblet cells are few in number and are apparently immature, being more nearly the shape of a spear-head than that of a goblet. Over the free surface of the goblet cell the cuticular border dips in away from the lumen and cilia are absent. No goblet cells were observed that were in the process of extruding mucin. Goblet cells are not found below the origin of bronchus L2.

This ciliated pseudo-stratified type of epithelium lines the entire extent of the stem bronchus and continues out along the branches of the tracheo-bronchial tree as far as the sixth or seventh generation of tubules. In these generations the intermediate cells are not numerous and soon disappear entirely. From the sixth or seventh generation to and including the tenth generation the epithelium is ciliated pseudo-stratified consisting of two cell types, the pyramidal basal cells with irregular smaller darkly staining nuclei and scant cytoplasm and the slender ciliated cells with oval or flattened nuclei placed at right angles to the cuticular border. These ciliated cells extend down between the basal cells with tapering ends and the cytoplasm is more abundant at the cuticular pole of the cell.

The epithelium is not ciliated beyond the tenth generation of tubules. In other respects it is like that of generations 6 or 7 to 10 as far as generation 13. In the case of both D1 and L1 the origin of generation 14 is marked by an abrupt change of the epithelium to a simple cuboidal type. In vertical section the outline of these cells is practically square. The nucleus is large, round and centrally placed with fine scattered chromatin granules. The cytoplasm takes a moderate amount of stain and appears structureless. In generations 15, 16 and 17 the cytoplasm is more abundant, seems rarefied, stains lightly, and the nuclei are much more vesicular. This peculiar condition of the cells of the smaller tubules has been noted by Dogliotti and Amprino (16).

In all the regions examined throughout the entire tree the epithelium forms a continuous lining from trachea to the blind ends of the terminal generations. At no point was there any evidence of a break in the epithelial lining or of local death of tissue. No areas were observed in which parts of the lining cells were being desquamated.

2. *Basement Membrane.*

The basement membrane of the oral end of the tree is thicker than in the smaller divisions. The epithelial cells rest directly on the reticulum fibers of the stroma throughout the extent of the tubular system, and the basement membrane is intact throughout.

3. *Glands.*

The tracheal glands are very numerous and are of a compound tubulo-alveolar type. In the alveoli two types of glandular cells are found, namely, cuboidal granular cells of a serous nature and columnar mucin containing cells. In the trachea typical crescents of Giannuzzi were noted. The ducts, near the alveoli, are lined with a cuboidal epithelium, but the lining becomes pseudostratified near the orifices of the ducts. The stem bronchus contains fewer glands than the

trachea and the alveoli of the glands consist almost entirely of serous cells. As the branches of the stem bronchus are followed outward, glands are present as far as and including the seventh generation. In the smaller tubules many of the glands are still in a simple tubular stage.

4. *Cartilage.*

In the trachea several of the C-shaped rings are completely formed, while in the bronchi the cartilage is present in the form of plates. The cartilage extends out as far as and including the eighth generation of branchings.

B. STROMA OF THE LUNG

The stroma consists of fibroblasts rather loosely and irregularly arranged between the tubules. In the walls of the first eight generations of bronchi, chondroblasts and the appearance of cartilage are noted. There is no particular condensation of the stroma about the walls of the remaining generations of tubules. The stroma lying between the terminal ramifications is quite avascular. This observation is contrary to that of Rose, but is supported by the studies of Dogliotti. A high power microscopic field of the lung tissue resembles that of a compound tubular gland in many ways, although the stroma is relatively great in amount in the lung at this stage. Studies of areas in which no large bronchi or vessels are present show that the stroma makes up about 79% of the mass of the pulmonary tissue. Free cells are very occasional in the stroma and seem to be of the cell type usually described as clasmatocytes.

C. LYMPH GLANDS

The largest of the lymph glands have a typical peripheral sinus but there are no secondary nodules or "germinal centers" present. The gland is made up of closely packed cells which appear to be large lymphocytes for the most part. However, there are considerable numbers of free polymorphonuclear cells. The lymph glands appear relatively vascular.

No peculiar histologic characteristics at this stage were noted in the other structures described in the section on Morphology.

V. SUMMARY

1. The bronchial tree of a human foetus of 152 millimeter length (c. r.) has a continuous intact lining of epithelium.

2. According to a method of enumeration outlined, there are seventeen generations of tubules present as a maximum number. In such a location the first thirteen generations are lined by a pseudo-stratified epithelium, the remaining four generations have a cuboidal epithelium.

3. In the terminal generations of tubules (last two or three) the epithelial cells are relatively large, with round vesicular nuclei and abundant cytoplasm that appears to be rarefied.

4. The terminal tubules have a diameter of 0.05 to 0.06 millimeter.

5. The more oral the site of origin of a branch bronchus from the stem bronchus the greater the number of generations of tubules that have arisen from this branch bronchus.

6. When viewed from above, there is a marked clock-wise rotation of the stem bronchus in its course.

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I am indebted to Professor R. A. Knouff, who suggested this problem; to Miss Thelma Baird, who prepared the serial sections, and to Miss Florence Melvin, who prepared the illustrations.

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EXPLANATION OF PLATES

PLATE I

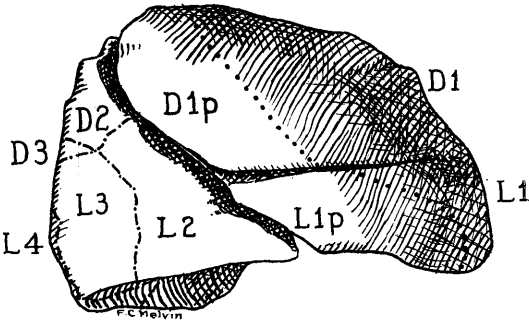
Right Lung. Surface areas of bronchial distribution. Lateral, Dorsal, Medial and Diaphragmatic views of a wax reconstruction.

Areas: D1, First Dorsal Bronchus except its first branch which is indicated by D1p. L1, First Lateral Bronchus except its first branch which is indicated by L1p. Other dorsal bronchi, D2, D3 and D4. Other lateral bronchi, L2, L3 and L4. V1, First Ventral Bronchus (Infracardial bronchus). Tr., Trachea. RSB, Right Stem Bronchus. X 2.

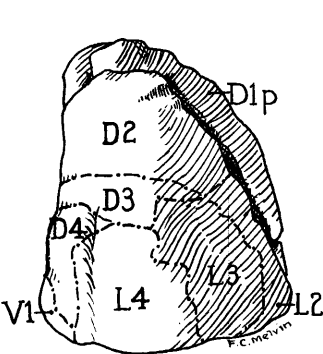
PLATE II

Semidiagrammatic sketches of epithelium of tracheo-bronchial tree.

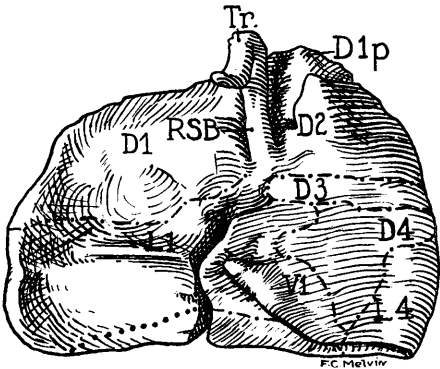
G, Goblet cell; CI, Ciliated cell; I, Intermediate cell; B, Basal cell; CO, Nonciliated columnar cell; CU, Cuboidal cell; L. CU, Light-staining cuboidal cell. X 550.



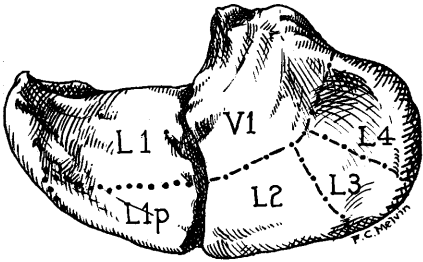
Lateral



Dorsal



Medial



Diaphragmatic

